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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,481	03/11/2005	John Beresford Davis	P33107	5730

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EXAMINER	
YOUNG, HUGH PARKER	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 10/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/527,481	DAVIS ET AL.	
	Examiner	Art Unit	
	Hugh P. Young	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *3-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 03/11/2005
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is the first Office action on the merits of application No. 10/527,481. Claims 1 – 9 are pending, with claims 1, 2, and 7 – 9 under consideration.

Election/Restriction

1. Applicant's election with traverse of Group I, Claims 1, 2, and 7-9, in the reply filed on August 11, 2006 is acknowledged. Applicant did not recite any particular grounds for traversal and the Examiner restates the justification for the original restriction as follows: the vanilloid receptor antagonists that are claimed as the unifying basis of the claims are known in the art. Furthermore, the different diseases or medical conditions encompassed by each of the groups of claims would be an undue search burden, given their different status in the art and non-overlapping patient populations.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1, 2, 7, and 9 are rejected under 35 U.S.C. 102(e) as being anticipated in a PCT publication by Bakthavatchalam et al., WO/2002/008221. Bakthavatchalam et al. teach the use of compounds that bind with the capsaicin receptors, including the human VR-1 receptor. They disclose high-affinity binding antagonists as well as pharmacological preparations of the same for the treatment of diseases and conditions, involving chronic and acute pain (a symptom of kidney stones or renal colic) in the Abstract. The last paragraph of page 2 of the Disclosure teaches the use of VR-1 antagonists for treating patients suffering from diseases or conditions that involve pain or urinary incontinence, both of which are symptoms typical of passage of or blockage by kidney stones. The instant application claims use of a vanilloid receptor antagonist in claims 1, 2, 7 and 9 for treatment or prophylaxis of several medical conditions, of which renal colic was elected after restriction. These claims are thus anticipated by Bakthavatchalam et al.

4. Claims 1, 2, 7, and 9 are rejected under 35 U.S.C. 102(e) as being anticipated in a PCT publication by Suh et al., WO/2002/016317. Suh et al. teach the use of compounds that are antagonists of VR-1 receptors. They disclose high-affinity binding antagonists as well as pharmaceutical preparations of the same for the treatment of chronic and acute pain, both of which are characteristic of passage of kidney stones (renal colic), and urinary bladder hypersensitivity, as well as inflammatory conditions of mucous membranes. These medical conditions are claimed in Suh et al's claims 3 and 4, for pharmaceutical compositions and methods of treating the conditions, respectively, as well as being recited in the Abstract. Claim 5 of Suh et al. claims vanilloid receptor

antagonism as the functional mechanism. The compounds are disclosed as broadly acting on nervous and mucosal sites that contain vanilloid receptors, which includes VR-1 receptors. The instant application claims use of a vanilloid receptor antagonist in claims 1, 2, 7 and 9 for treatment or prophylaxis of several medical conditions, of which renal colic was elected after restriction. These claims are thus anticipated by Suh et al.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claim 9 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 8, 9, 10, 11, and 12 of copending Application No.10/540,100. Although the conflicting claims are not identical, they are not patentably distinct from each other because they disclose and claim methods of using the same chemical structure, the vanilloid VR-1 receptor antagonist N-(2-Bromophenyl)-N'-[(R-1-(5-trifluoromethyl-2-pyridyl)pyrrolodin-3-yl)]urea, explicitly claimed in claim 8 of the instant application and in claims 9, 10, and 11 of the 10/540,100 application. The species, N-(2-Bromophenyl)-N'-[(R-1-(5-trifluoromethyl-2-pyridyl)pyrrolodin-3-yl)]urea, claimed in the instant application anticipates the methods of claims 1 – 11 of the copending application, 10/540,100, that use VR-1 antagonists. The pharmaceutical composition of the instant claim 9 is rendered obvious in light of the fact that one would have to have the specific compound claimed in the copending application. Furthermore, claim 12 of copending application 10/540,100 claims a

pharmaceutical composition comprising a vanilloid receptor (VR-1) antagonist, or pharmaceutically suitable composition thereof, for which the compound used in the methods of claims 1 – 11 is obviously available as the material of claim 12.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 2, 7, 8, and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of renal colic, does not reasonably provide enablement for prophylaxis or prevention of same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the method of use of the invention commensurate in scope with these claims. In the instant case the term prophylaxis is interpreted broadly as meaning prevention, in this case prevention of renal colic. Although the invention as disclosed and claimed is enabled for treating, that is, alleviating, ameliorating or abating the pain associated with renal colic, it does not go so far as to completely eliminate the condition in terms of both time, either onset or duration, or intensity.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation. The factors follow:

1. *the nature of the invention*; Methods for prophylaxis or prevention of renal colic.

2. *the breadth of the claims*; Treatment and prophylaxis, or prevention, of renal colic or pain associated with the condition is claimed without any strictures as to any thresholds for either the amount of time elapsing before the effect of the medicament occurs or a levels of sensation that would constitute complete absence of pain.

3. *the predictability or unpredictability of the art*; Alleviation of pain is very unpredictable. Bortolloti et al. (2002; *Aliment. Pharmacol. Therap.* 16:1075-1082) teach that pain associated with vanilloid receptors can be alleviated in some, but not all, patients and that furthermore many patients report a worsening of pain at the outset of treatment that is followed only later by abatement of sensation (see Discussion, page 1081). Szallasi et al. (1993; *J. Pharmacol. Exper. Therapeut.* 267; 728-733) teach that vanilloid receptors occur in several subtypes that differ in both physical location throughout the body but in relative sensitivity to different binding agents, whether agonists or antagonists (see Discussion, page 732-733).

4. *the amount of direction or guidance presented*; The instant disclosure provides no guidance to indicate what criteria would lead one to use the invention on a given patient or what signs or symptoms would allow a practitioner to apply a suitable

dose. No working examples are recited in the disclosure. The references cited in item 3 above indicate that the nature of both the medical condition, pain, and the physical mechanisms for the origin of the sensation of pain are both variable and unpredictable. The instant disclosure is silent with respect to what means one would use to assess the presence or intensity of the medical problem and the appropriate level of response to be provided application of the invention.

5. *the presence or absence of working examples*; The instant disclosure does not provide working examples that would allow one to predict how or when to use the invention. Both formulation of the medicament and criteria for the use of same are not disclosed in detail.

6. *the quantity of experimentation necessary*; The actual composition to be used and even the route of entry into the patient's body of the active principle are not disclosed except in general terms applicable to most pharmacological preparations. Any real, concrete material suitable for use as a medical or veterinary treatment is left to the practitioner to determine by experiment or trial. One wishing to practice the invention would have to perform extensive experiments in order to determine dosage levels and frequencies that would be both safe and effective for either humans or animals. Lack of data from even basic in vitro laboratory experiments leaves anyone attempting to practice the invention faced with the necessity of performing fundamental dose response experiments in order to have even a general idea as to how to make and use the medicaments claimed.

7. *the state of the prior art;* As indicated in items 1 – 6 above, the field of pain alleviation is very broad and grounded in concrete results of actual practice and controlled experimental trials, with little reliance being placed on projections from theoretical models. The variability of the causes of the underlying medical condition, pain, the variability of the different physiological organs and systems in which pain is sited, the variability of the different neural receptors and the chemical species active upon them, and finally the variability of different patient populations all indicate that considerable guidance is needed beyond the established art in this field.

8. *the relative skill of those skilled in the art;* In view of the discussion of each of the preceding seven factors the level of skill in this art is high and is at least that of a medical doctor or doctor of pharmacology with several years of experience in the art. As the cited art would point to, even with a level of skill in the art which is high, predictability of the results is not invariable.

In consideration of each of factors 1 - 8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue in light of the lack of a comprehensive written description.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hugh P. Young whose telephone number is (571)-272-4988. The examiner can normally be reached on 8:00 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hugh Parker Young Ph.D. GAU 1654